More Concerns for Farmers

Neurologic Effects of Chronic Pesticide Exposure

Farm field fallout. A recent analysis shows that even moderate chronic pesticide use can result in neurologic symptoms among farmers and other applicators.

Corbis

Although there is considerable evidence that pesticides are neurotoxic, most research has focused on the short- and long-term consequences of acute high-level exposure such as that seen during industrial accidents or food contamination. To date, little has been known about the effects of chronic moderate exposure such as that experienced by farmers and other workers who regularly use agricultural pesticides. Now, a recent analysis of data collected in the Agricultural Health Study (AHS) links chronic moderate pesticide exposure to neurologic symptoms affecting both the central and peripheral nervous systems [*EHP* 113:877–882]. According to the research team, increases in such symptoms may be an early indicator of impaired neurological function.

The AHS, an ongoing study sponsored by the NIEHS, the National Cancer Institute, and the U.S. Environmental Protection Agency, furnished a rich data source for the researchers to investigate possible links. Between 1993 and 1997, approximately 20,000 private pesticide applicators (primarily farmers) in Iowa and North Carolina enrolled in the AHS and completed two questionnaires on demographic characteristics, lifestyle, medical history (including neurologic symptoms), and pesticide use. The current analysis focused on 18,782 of these individuals, white men aged 18–75 years who provided complete symptom information.

The 23 symptoms in the analysis included headache, dizziness, depression, limb weakness, poor balance, difficulty concentrating, and vision difficulties. In addition to the symptom information, participants detailed how long and how frequently they used any of 50 pesticides, including insecticides, herbicides, fungicides, and fumigants. They also indicated whether they had ever experienced pesticide poisoning or high-exposure incidents such as accidental skin contact with a large amount of pesticide.

To define cumulative exposure, the researchers calculated lifetime days of use from the number of years and the number of days per year that the applicators had used each pesticide. The team considered two measures of symptoms: the absolute number and the presence of 10 or more. To control for confounding by pesticide poisoning or high-exposure incidents, the researchers conducted analyses with and without those data from affected individuals. They also considered potential effects from pesticide use within the past year.

For pesticides overall, applicators with the most (more than 500) cumulative lifetime days of pesticide use reported more symptoms than those with the fewest lifetime days of use. The relationship between cumulative exposure and symptoms was strongest with insecticides; applicants with the most lifetime days of use were 2.5 times more likely to have 10 or more symptoms as applicators who had never used insecticides. Within the insecticide category, relationships with symptoms were strongest for organophosphates and organochlorines. Neither recent use nor a history of poisoning or high-exposure incident affected the results.

The results of this study extend previous research demonstrating a link between chronic moderate pesticide exposure and a range of cognitive, sensory, and motor symptoms. The AHS is unusually robust due to its large size and its wealth of detailed exposure information. The results of this analysis provide substantial evidence that neurologic symptoms may be increased by even moderate insecticide exposure, and that cumulative exposure may be as important as recent exposure, although more work is needed to understand the pathology underlying the reported symptoms. **–Julia R. Barrett**

Blocking Brain Development

How PCBs Disrupt Thyroid Hormone

Polychlorinated biphenyls (PCBs) have long been known to alter growth and development in animals and humans, and are suspected of interfering with the action of thyroid hormone (TH) in humans. Much less is known about which congeners of this large chemical family may have such action and how they interfere with TH. Now, in an *in vitro* study using human brain stem cells, a team of German and Californian researchers shows how a specific PCB congener, PCB-118, can interrupt normal TH function and cause the premature differentiation of one type of brain cell [*EHP* 113:871–876].

Many animal studies, primarily in rats, suggest that PCBs can profoundly affect fetal brain development, which itself is highly dependent on the availability and amount of TH, principally from the mother. PCBs are known to lower circulating blood levels of TH by increasing TH metabolism and binding to TH transport proteins; the exact mechanisms and effects of TH disruption by

PCBs are unclear, however. Some epidemiologic evidence suggests a link between PCB exposure during fetal development and subsequent cognitive problems in children, such as lowered overall IQ, attention and motor deficits, and impaired impulse control. The suspicion that these problems may be related to PCBs' effects on the timing and type of brain cell differentiation led to the current study.

Stem cells known as normal human neural progenitor (NHNP) cells develop into three types of brain cells: neurons, which receive and transmit electrical signals via axons and synapses; astrocytes, which manage neurons' surrounding environment; and oligodendrocytes, which produce myelin, the fatty sheath that insulates axons. TH is known to control the timing of oligodendrocyte differentiation.

The research team exposed NHNP cells to two PCB congeners—PCB-118 and PCB-126—and observed the effects on cell differentiation. They found that cells exposed to PCB-118 prematurely turned into oligodendrocytes. This finding suggests strongly that PCBs may facilitate the binding of coactivator proteins to cellular TH receptors; these proteins then mimic the action of TH. Paradoxically, a surplus of oligodendrocytes early in brain development may lead to a dearth later, because if there are proportionally fewer neurons, many oligodendrocytes cannot wrap an axon or reproduce. In that case, they undergo apoptosis, or programmed cell death. The end result would likely be a drop in the total number of brain cells.

The current study is consistent with an earlier rat study published in the April 2004 issue of *EHP*, which found that PCBs interfered directly with fetal TH receptor signaling, as opposed to reducing circulating maternal TH levels. Like many other studies, that study used Aroclor 1254, a commercial mixture of several PCB congeners, and did not determine the effects of each congener. The current study compared two PCB congeners that differ somewhat in their toxic equivalence (TEQ). The results showed that the lower-TEQ congener (PCB-118) acted via the TH pathway while the higher-TEQ congener (PCB-126) did not. The apparent toxicity of a PCB congener with a low TEQ also suggests that the TEQ system may not be a reliable measure of all types of toxicity. **–Valerie J. Brown**

Questioning Lead Standards

Even Low Levels Shave Points off IQ

The maximum blood lead concentration deemed acceptable for children has declined over the years, from 60 micrograms per deciliter (µg/dL) in 1970 to the present-day level of 10 µg/dL, first established in 1991. In the last several years, however, researchers have begun to suspect that even lower concentrations may impair cognition. Now a reevaluation of data from seven international longitudinal studies involving 1,333 children confirms this suspicion [*EHP* **113:894–899**].

The studies—conducted in Boston, Cincinnati, Cleveland, Rochester (New York), Port Pirie (Australia), Mexico City, and Yugoslavia—originally looked at children known to be at risk for lead poisoning, such as those living near lead smelters or in deprived urban settings. Therefore, the majority of the participants had blood lead levels far higher than the averages currently being reported in the developed world. The mean blood lead concentration for the entire group peaked at 17.8 µg/dL at age 2.5 years,

Image Source

The test of time. More studies are confirming the surprise finding that blood lead concentration at the time of IQ testing, not peak level, is a better predictor of IQ effects.

and declined to 9.4 µg/dL between ages 5 and 7. Only 18% of the children had maximal blood lead levels of less than 10 µg/dL, and 8% had maximal blood lead levels of less than 7.5 µg/dL.

Most of the children took IQ tests when they were between almost 5 and 7 years of age; the Boston children were tested at age 10. The current team calculated, across the seven studies, how much of the difference in IQ scores was related to lead alone by controlling for other factors that influence IQ scores, including child birth weight, birth order, prenatal exposure to tobacco smoke and alcohol, and mother's IQ.

On a population basis, an increase in blood lead level from 2.4 to 10 µg/dL at the time of testing was associated with a decrease of 3.9 IQ points. At lower blood lead levels, a small increase in blood lead made a bigger difference in IQ than the same size increase did at higher concentrations. A blood lead level of 20 µg/dL was associated with scoring about 1.9 points lower on tests of IQ compared with a blood lead level of 10 µg/dL. The difference in IQ shrank to 1.1 points when comparing a blood lead level of 20 µg/dL with a concentration of 30 µg/dL.

To determine if the data from one particular study drove the final results, the team removed the findings for one site at a time and recalculated the results. It became clear that no single study was driving the results of the pooled analysis.

Consistent with a study published in the May 2005 issue of *EHP*, blood lead level at the time of IQ testing was generally a stronger predictor of effects on IQ than was—as previously believed—blood lead level at age 2. The individual-level effect on IQ is difficult to determine, however, and may depend in part on the child's social environment.

In the United States, about 2–3% of children have a blood lead concentration above 10 µg/dL, but in some cities, such as Rochester, 1 in 5 children have elevated blood lead. These new findings, along with those from previous human and animal studies, point to the importance of eliminating nonessential uses of lead and lowering allowable levels of lead in air emissions, house dust, soil, water, and consumer products. **–Tina Adler**

Tap Water and Trihalomethanes

Flow of Concerns Continues

Trihalomethanes (THMs) are the result of a reaction between the chlorine used for disinfecting tap water and natural organic matter in the water. At elevated levels, THMs have been associated with negative health effects such as cancer and adverse reproductive outcomes. Now a study by government and academic researchers adds to previous evidence that dermal absorption and inhalation of THMs associated with everyday tap water use can result in significantly higher blood THM concentrations than simply drinking the water does [*EHP* **113:863–870**]. The results of this exposure assessment study could serve as a guide for future epidemiologic investigations exploring the potential connection between THMs in tap water and adverse health effects.

The researchers recruited seven healthy participants aged 21–30 years to spend two 24-hour periods (usually one week apart) in one of two study residences. The study residences were typical ranch-style homes, one located in North Carolina, the other in Texas. The North Carolina house was served with a water supply higher in THMs than that of the Texas house.

Over the total two days, each participant performed 14 activities using tap water. These included drinking a hot beverage prepared with tap water (THM-free bottled water was consumed except when drinking was part of a test activity), washing their hands, showering, washing dishes both by hand and in a dishwasher, and washing clothes in a washing machine. The water use activities were rigidly scheduled and controlled for exposure time and water temperature.

The team took baseline measurements of the THMs in ambient indoor air, cold tap water, and subjects' blood and exhaled breath just before and just after each activity. The ratio between pre- and post-activity measurements illustrated the impact of each activity on participants' blood and exhaled breath THM concentrations; twofold or greater deviation from baseline was established as meaningful.

Relatively high pre- to postactivity ratios were observed for several of the activities. For example, blood concentrations rose 5- to 15-fold as a result of showering in the North Carolina participants, and rose approximately 5-fold in the Texas subjects. The results confirm that showering and bathing are important sources of THM exposure; they also provide evidence that other THM exposure scenarios, such as washing dishes by hand and being exposed to a cohabitant's shower steam, may also be important.

Although an apparent dose–response relationship was discovered, the authors emphasize that public health implications should not be inferred from their findings, partly due to the small number of subjects. Their purpose was to shed light on which water use activities should be considered in the context of an epidemiologic study and to establish some practical approaches for future investigations. Noting the wide range in blood THM concentrations among the subjects in this and other studies in response to similar levels of THM exposure, subsequent exposure assessment research is being conducted on the possibility that genetic variation may play a role in individuals' susceptibility to absorption of THMs. **–Ernie Hood**

Pierre Wagner/Alamy

Are shower buffs in hot water? Household uses of hot tap water such as showering and dish washing result in greater THM absorption than simply drinking the water.